

IN THE CLAIMS

1 (Original). A method of stimulating secretion of an ATP-independent cytotoxic factor from a pathogenic microorganism comprising the steps of:

- (a) providing a growth medium comprising a mammalian protein;
- (b) growing the pathogenic microorganism in the growth medium; and
- (c) allowing the pathogenic microorganism to secrete the ATP-independent cytotoxic factor in the presence of the protein.

2 (Original). The method of claim 1 wherein the mammalian protein is selected from the group consisting of kappa casein, bovine serum albumin, ovalbumin, and α 2-macroglobulin.

A1
3 (Original). A method of delineating virulent and avirulent microorganisms comprising the step of identifying the presence of receptors for mammalian proteins on the surface of the microorganisms.

4 (Original). The method of claim 3, wherein the mammalian proteins are selected from a group consisting of kappa casein, bovine serum albumin, ovalbumin, and α 2-macroglobulin.

5 (Original). A method of isolating an ATP-independent cytotoxic factor from a pathogenic microorganism, comprising:

- (a) providing a growth medium comprising a mammalian protein;
- (b) growing the pathogenic microorganism in the growth medium;

- (c) allowing the pathogenic microorganism to secrete cytotoxic factors in the presence of the mammalian protein;
- (d) removing the pathogenic microorganism to produce a substantially cell free growth medium; and
- (e) purifying the substantially cell free growth medium by one or more chromatographic steps.

6 (Original). The method of claim 5, wherein, one of the chromatographic steps comprises isolating the cytotoxic factor as the flow-through fraction from an ion-exchange column.

A/

7 (Original). The method of claim 6, wherein the ion-exchange column comprises of an anion exchanger.

8 (Currently amended). The method of claim 6, wherein the ion-exchange column comprises of ~~an~~ a cation exchanger.

9 (Original). The method of claim 7, wherein the anion exchanger is selected from a group consisting of diethylaminoethyl, quaternary aminoethyl and quaternary ammonium.

10 (Original). The method of claim 8, wherein the cation exchanger is selected from a group consisting of carboxymethyl, sulphopropyl and methyl sulphonate.

11 (Original). The method of claim 5, wherein the chromatographic steps comprise a hydroxyapatite chromatography step, an affinity chromatography step and an ion-exchange chromatography step.

12 (Original). The method of claim 5, wherein the chromatographic steps comprise:

- (a) isolating the flow-through fraction of the growth medium from a hydroxyapatite column;
- (b) passing the flow-through fraction from the hydroxyapatite column down an ATP affinity column;
- (c) isolating the flow-through fraction from the ATP affinity column;
- (d) passing the flow-through fraction from the ATP affinity column down an ion-exchange column; and
- (e) isolating the cytotoxic factor as the flow-through fraction from the ion-exchange column.

13 (Currently amended). The method of claim 12, wherein the ATP affinity column is a an ATP-agarose column.

14 (Original). The method of claim 12, wherein the ion-exchange column is a Q-sepharose column.

15 (Original). The method of claim 1, wherein the cytotoxic factor is a redox protein factor.

16 (Original). The method of claim 5, further comprising testing the purified growth medium to detect ATP-independent apoptosis-triggering activity.

17 (Original). A method of treating a condition related to resistance to cell death, comprising administering a substantially pure cytotoxic factor, or a variant or derivative thereof, optionally incorporated in a pharmaceutical carrier, to promote cell death in a cell demonstrating resistance to cell death.

18 (Original). The method of claim 17 wherein the condition related to resistance to cell death is selected from the group consisting of human melanoma, leukemia, breast cancer, ovarian cancer, lung cancer, mesenchymal cancer, colon cancer and aerodigestive tract cancers.

AI

19 (Original). The method of claim 18 wherein the pharmaceutical carrier is selected from the group consisting of a filler, a cellulose preparation, a flavoring agent, a coloring agent, a thickener, a detackifier, an additive, a binder, an adjuvant, and mixtures thereof.

20 (Original). The method of claim 18 wherein the cytotoxic factor is administered orally, buccally, by inhalation, sublingually, rectally, vaginally, transurethrally, nasally, topically, or percutaneously.

21 (Original). A method of treating a condition related to cell death susceptibility, comprising the step of administering a therapeutically effective amount of an inhibitor of a cytotoxic factor, or a derivative thereof, optionally incorporated in a

pharmaceutical carrier, to inhibit cell death in a cell demonstrating susceptibility to cell death.

22 (Original). The method of claim 21 wherein the inhibitor is selected from the group consisting of:

- (a) an active agent that inhibits secretion of an ATP-utilizing enzyme,
- (b) an active agent that inhibits the cytotoxic activity of an ATP-utilizing enzyme,
- (c) an active agent that inhibits secretion of a redox protein, and
- (d) an active agent that inhibits the cytotoxic activity of a redox protein.

A/ 23 (Original). A method of modulating a rate of cell death, comprising the step of administering a compound selected from the group consisting of a substantially pure cytotoxic factor, an inhibitor of a substantially pure cytotoxic factor, an activator of a substantially pure cytotoxic factor, and a variant or derivative of said cytotoxic factor, inhibitor, and activator.

24 (Original). The method of claim 23 wherein the cytotoxic factor is selected from the group consisting of an ATP-utilizing enzyme, a redox protein, an activator of ATP production, and an inhibitor of ATP-production.

25 (Original). A method of treating a condition related to resistance to cell death in a host organism comprising the step of administering a composition comprising a substantially pure cytotoxic factor, or a variant or derivative thereof, in an amount sufficient to stimulate a natural immune response in the host organism.

26 (New). The method of claim 17, wherein the cytotoxic factor is azurin or cytochrome C₅₅₁.

27 (New). The method of claim 26, wherein the cytotoxic factor is azurin.

28 (New). The method of claim 26, wherein the cytotoxic factor is cytochrome C₅₅₁.

29 (New). The method of claim 23, wherein the cytotoxic factor is azurin or cytochrome C₅₅₁.

30 (New). The method of claim 29, wherein the cytotoxic factor is azurin.

31 (New). The method of claim 29, wherein the cytotoxic factor is cytochrome C₅₅₁.
